

This listing of claims will replace all prior versions of claims in the application:

Listing of Claims: Please amend the claims as follows:

We claim:

Claims 1.–39. (Cancelled)

Claim 40. (Withdrawn) A pharmaceutical composition comprising a DG001 protein and/or a functional fragment thereof, a nucleic acid molecule encoding a DG001 protein and/or a functional fragment thereof and an effector/modulator of said nucleic acid molecule and/or said protein or protein fragment, wherein the composition optionally contains pharmaceutically acceptable carriers, diluents, and/or additives.

Claim 41. (Withdrawn) The composition of claim 40, wherein the nucleic acid molecule is a mammalian DG001 nucleic acid, particularly encoding the human DG001 polypeptide and/or a nucleic molecule which is complementary thereto or a fragment thereof or a variant thereof.

Claim 42. (Withdrawn) The composition of claim 41, wherein said nucleic acid molecule is selected from the group consisting of (a) a nucleic acid molecule encoding a polypeptide as shown in SEQ ID NO: 2, or an isoform, fragment or variant of the polypeptide as shown in SEQ ID NO: 2; (b) a nucleic acid molecule which comprises or is the nucleic acid molecule as shown in SEQ ID NO: 1; (c) a nucleic acid molecule being degenerate with as a result of the genetic code to the nucleic acid sequences as defined in (a) or (b); (d) a nucleic acid molecule that hybridizes at 50.degree. C. in a solution containing 1.times.SSC and 0.1% SDS to a nucleic acid molecule as defined in claim 41 or as defined in (a) to (c) and/or a nucleic acid molecule which is complementary thereto; (e) a nucleic acid molecule that encodes a polypeptide which is at least 85%, preferably at least 90%, more preferably at least 95%, more preferably at least 98% and up to 99.6% identical to the human DG001, as defined in claim 41 or to a polypeptide as defined in (a); (f) a nucleic acid molecule that differs from the nucleic acid molecule of (a) to (e) by mutation and wherein said mutation causes an alteration,

deletion, duplication or premature stop in the encoded polypeptide

Claim 43. (Withdrawn) The composition of claim 40, wherein the nucleic acid molecule is a DNA molecule, particularly a cDNA or a genomic DNA.

Claim 44. (Withdrawn) The composition of claim 40, wherein said nucleic acid molecule is a recombinant nucleic acid molecule and wherein the polypeptide is a recombinant polypeptide, particularly a fusion polypeptide.

Claim 45. (Withdrawn) The composition of claim 40, wherein the nucleic acid molecule is a vector, particularly an expression vector.

Claim 46. (Withdrawn) The composition of claim 40, wherein said nucleic acid molecule is selected from hybridization probes, primers and anti-sense oligonucleotides.

Claim 47. (Withdrawn) The composition of claim 40 which is a diagnostic and/or a therapeutic composition.

Claim 48. (Withdrawn) The composition of claim 40 for the manufacture of an agent for (i) detecting and/or verifying, for the treatment, alleviation and/or prevention of pancreatic diseases (e.g. diabetes such as insulin dependent diabetes mellitus and/or non-insulin dependent diabetes mellitus), obesity, metabolic syndrome and/or other metabolic diseases or dysfunctions, (ii) the modulation of pancreatic development, and/or (iii) the regeneration of pancreatic tissues or cells, particularly pancreatic beta cells.

Claim 49. (Withdrawn) The composition of claim 40 for application *in vivo* or *in vitro*.

Claim 50. (Currently Amended) A method for the treatment of diabetes or obesity, ~~metabolic syndrome or a method for the treatment of a metabolic disease or metabolic dysfunction~~, comprising administering to a subject in need thereof, a human pleiotrophin polypeptide or a functional fragment thereof.

Claim 51. (Withdrawn) Use of a DG001 nucleic acid molecule or use of a polypeptide encoded thereby, or use of a fragment or a variant of said nucleic acid molecule or said polypeptide, or use of an effector/modulator of said nucleic acid molecule or said polypeptide for identifying substances capable of interacting with a DG001 polypeptide *in vitro* and/or *in vivo*.

Claim 52. (Withdrawn) A non-human transgenic animal exhibiting a modified expression of a DG001 polypeptide, particularly wherein the expression of the DG001 polypeptide is increased and/or reduced.

Claim 53. (Withdrawn) A recombinant host cell exhibiting a modified expression of a DG001 polypeptide, or a recombinant host cell which comprises a nucleic acid molecule as defined in claim 40, wherein the host cell is particularly a human cell.

Claim 54. (Withdrawn) A method of identifying a (poly)peptide involved in the regulation of energy homeostasis and/or metabolism in a mammal comprising the steps of (a) contacting a collection of (poly)peptides with a DG001 homologous polypeptide or a fragment thereof under conditions that allow binding of said (poly)peptides; (b) removing (poly)peptides which do not bind and (c) identifying (poly)peptides that bind to said DG001 homologous polypeptide.

Claim 55. (Withdrawn) A method of screening for an agent which effects/modulates the interaction of a DG001 polypeptide with a binding target comprising the steps of (a) incubating a mixture comprising (aa) a DG001 polypeptide or a fragment thereof; (ab) a binding target/agent of said DG001 polypeptide or fragment thereof; and (ac) a candidate agent under conditions whereby said polypeptide or fragment thereof specifically binds to said binding target at a reference affinity; (b) detecting the binding affinity of said DG001 polypeptide or fragment thereof to said binding target to determine an affinity for the agent; and (c) determining a difference between affinity for the agent and reference affinity.

Claim 56. (Withdrawn) A method for screening for an agent, which effects/modulates the activity of a DG001 polypeptide, comprising the steps of (a) incubating a mixture comprising (aa) a DG001 polypeptide or a fragment thereof; and (ab) a candidate agent under conditions whereby said DG001 polypeptide or fragment thereof exhibits a reference activity, (b) detecting the activity of said DG001 polypeptide or fragment thereof to determine an activity for the agent; and (c) determining a difference between activity for the agent and reference activity.

Claim 57. (Withdrawn) Use of a nucleic acid molecule as defined in claim 40 for the preparation of a medicament for (i) the treatment, alleviation and/or prevention of diseases or dysfunctions, including pancreatic diseases (e.g. diabetes), obesity, and/or metabolic syndrome, (ii) the modulation of pancreatic development, and/or (iii) the regeneration of pancreatic cells or tissues.

Claim 58. (Currently Amended) A method for the treatment of diabetes or obesity

~~(i) the treatment, alleviation or prevention of diabetes, obesity, or metabolic syndrome,~~

~~(ii) the modulation of pancreatic development, or~~

~~(iii) the regeneration of pancreatic cells or tissues~~

in a subject in need thereof, comprising administering to said subject a medicament comprising an acceptable carrier and a human pleiotrophin polypeptide or a functional fragment thereof.

Claim 59. (Withdrawn) Use of a DG001 nucleic acid molecule or of a fragment thereof for the production of a non-human transgenic animal which over- or under-expresses the DG001 gene product.

Claim 60. (Cancelled)

Claim 61. (Cancelled)

Claim 62. (Cancelled)

Claim 63. (Currently Amended) ~~The method according to claim 58, wherein said human pleiotrophin~~ A method for the treatment of diabetes or obesity in a subject in need thereof, comprising administering to said subject a polypeptide which is

- (a) a polypeptide comprising the sequence set forth in SEQ ID NO: 2, or a functional fragment thereof ~~an isoform, fragment or variant of the polypeptide of SEQ ID NO: 2;~~
- (b) a polypeptide encoded by the polynucleotide comprising the sequence set forth in SEQ ID NO: 1;
- (c) a polypeptide which is encoded by a polynucleotide which, as a result of the genetic code, is degenerate with the polynucleotide sequence of (b);
- (d) a polypeptide which is encoded by a polynucleotide which hybridizes at 50°C in a solution containing 1 x SSC and 0.1% SDS to the polynucleotide sequence of (b) or (c);
- (e) a polypeptide which is at least 85% identical to the polypeptide of (a); or
- (f) a polypeptide that differs from the polypeptide of (a) to (e) by a mutation in the polynucleotide sequence encoding said polypeptide, wherein said mutation causes an alteration, deletion, duplication or premature stop in the encoded polypeptide.

Claim 64. (Previously Presented) The method according to claim 58, comprising administering a human pleiotrophin polypeptide comprising the sequence set forth in SEQ ID NO: 2.

Claim 65. (Currently Amended) The method according to claim 58, wherein said diabetes is insulin dependent diabetes mellitus ~~or non-insulin dependent diabetes mellitus.~~

Claim 66. (Currently Amended) A method for generating insulin producing β cells, comprising

contacting a cell that expresses a pancreatic gene with an effective amount of human pleiotrophin polypeptide, ~~thereby producing~~ whereby said cell and its progeny differentiate into insulin producing β cells.

Claim 67. (Previously Presented) The method according to claim 66, comprising contacting a pluripotent stem cell that expresses a pancreatic gene with an effective amount of human pleiotrophin polypeptide.

Claim 68. (New) The method according to claim 63, wherein said human pleiotrophin polypeptide is

- (a) a polypeptide comprising the sequence set forth in SEQ ID NO: 2 or a functional fragment thereof;
- (b) a polypeptide encoded by the polynucleotide comprising the sequence set forth in SEQ ID NO: 1;
- (c) a polypeptide which is encoded by a polynucleotide which, as a result of the genetic code, is degenerate with the polynucleotide sequence of (b); or
- (d) a polypeptide which is at least 95% identical to the polypeptide of (a).

Claim 69. (New) The method according to claim 63, wherein said human pleiotrophin polypeptide is a polypeptide comprising the sequence set forth in SEQ ID NO: 2 or a functional fragment comprising 6 to 50 contiguous amino acids of said SEQ ID NO: 2.

Claim 70. (New) The method according to claim 58, wherein said diabetes is non-insulin dependent diabetes mellitus.